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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/276,455 | 03/25/1999 | ALAN ROY FERSHT | 674508-2001 | 2127 |

20999 7590 03/18/2005

FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

| EXAMINER | |
|---|---|
| ZEMAN, ROBERT A | |
| ART UNIT | PAPER NUMBER |
| 1645 | |

DATE MAILED: 03/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/276,455 | FERSHT ET AL. | |
| | Examiner | Art Unit | |
| | Robert A. Zeman | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,9-21,29-31 and 55-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9-21,29-31 and 55-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

The amendment filed on 12-6-2004 is acknowledged. Claims 1, 12-13 and 55-56 have been amended. Claims 57-61 have been added. Claims 1, 9-21, 29-31 and 55-61 are pending and currently under examination.

### *Claim Rejections Maintained and New Grounds of Rejection*

### *35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9-21, 29-31, 57 and 59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has amended claims 1, 12, 13, 57 and 59 to recite "wherein position 262 of said amino acid sequence or said corresponding sequence is occupied by an amino acid residue other than alanine, and wherein position 267 of said amino acid sequence or said corresponding sequence is occupied by an amino acid residue other than isoleucine". This phrase does not appear in the specification, or original claims as filed nor does Applicant point out specific basis for this limitation in the application, and none is apparent. The specification discloses, "GroEL fragments which conform to the database sequence are inoperative. Specifically, the database

contains a sequence in which positions 262 and 267 are occupied by Alanine and Isoleucine respectively. Fragments incorporating one or both of these residues at these positions are inoperative and unable to promote the folding of polypeptides. The invention, instead, relates to a GroEL polypeptide in which at least one of positions 262 and 267 is occupied by Leucine and Methionine respectively". This single embodiment does not lend support to the broad genus recited in the aforementioned claims. Therefore this limitation is new matter.

### *35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9-21, 29-31 and 55-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Braig et al. in view of Holland et al. for the reasons set forth in the previous Office action in the rejection of claims 1, 9-21, 29-31 and 55-56.

**Applicants argue**:

1. Braig et al. does not teach "fragments of GroEL" that have chaperone activity. Moreover, the skilled artisan would not have expected the said fragments to be functional chaperone polypeptides having refolding activity.

2. One would not have been motivated to make a recombinant *E. coli* GroEL fusion polypeptide.

3. Braig et al. do not disclose a sequence for GroEL wherein amino acid residue 262 is not an alanine and amino acid residue 267 is not isoleucine.

The instant claims are drawn to GroEL fragments with refolding activity, fusion proteins containing said fragments and compositions containing said fragments wherein position 262 of the claimed sequence is not alanine and position 267 is not isoleucine.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Points 1-3, Braig et al. disclose the entire amino acid sequence of *E. coli* GroEL (including fragments). While, Braig et al. does not explicitly disclose fragments with refolding activity wherein amino acid residue 262 is not an alanine and amino acid residue 267 is not isoleucine, some of said fragments would necessarily, in the absence of evidence to the contrary, possess refolding activity. Moreover, since the full-length polypeptide disclosed by

Braig et al. is biologically active it would not contain an alanine at position 262 or an isoleucine at position 267.

As stated previously, given that Braig et al. disclose the entire sequence of *E. coli* GroEL and that Holland et al. disclose a process of making a recombinant fusion polypeptide it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to identify the fragments of GroEL (including fragments with refolding activity) that have chaperone activity for use as a diagnostic tool. Moreover, one would have been motivated to utilize the method of Holland et al. to produce said fragments since the fusion proteins of Holland et al. are secreted into the culture medium thereby providing an efficient method for producing the GroEL polypeptides. One would have had a high degree of success since Holland et al. disclose that their method can be used for the production of a myriad of polypeptides including those of bacterial origin (see column 4, lines 10-12). Labigne et al. disclose the complete sequence for Hsp B (see Figure 7A). Said sequence is the same as SEQ ID NO:10.

Claims 1, 9-21, 29-31 and 55-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Labigne et al. (WO 94/26901) for the reasons set forth in the previous Office action in the rejection of claims 1, 9-21, 29-31 and 55-56.

The instant claims are drawn to GroEL fragments with refolding activity, fusion proteins containing said fragments and compositions containing said fragments wherein position 262 of the claimed sequence is not alanine and position 267 is not isoleucine.

**Applicant argues:**

1. The skilled artisan would not have expected the fragments of the present invention to be functional chaperone polypeptides having refolding activity.

2. Labigne et al. do are not concerned with refolding activity but with immunogenic fragments.

3. Labigne et al. do not disclose a sequence for GroEL wherein amino acid residue 262 is not an alanine and amino acid residue 267 is not isoleucine.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 1, Applicant seems to be arguing the claimed invention being predicated on "unexpected results" but provides no factual basis for said assertion. Hence it is deemed non-persuasive.

With regard to Points 2-3, Labigne et al. disclose the complete sequence for Hsp B (see Figure 7A). Said sequence is the same as SEQ ID NO:10. Labigne et al. further disclose fragments and fusion proteins of said proteins (see abstract and page 4). While, Labigne et al. does not explicitly disclose fragments with refolding activity wherein amino acid residue 262 is not an alanine and amino acid residue 267 is not isoleucine, some of said fragments would necessarily, in the absence of evidence to the contrary, possess refolding activity. Moreover, since the polypeptide disclosed by Labigne et al. is biologically active it would not contain an alanine at position 262 or an isoleucine at position 267.

***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Zeman
March 10, 2005

L. F. Smith

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600